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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,163	07/03/2003	Peter David Davis	215233.00107	4150

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EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 09/15/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/612,163	DAVIS, PETER DAVID	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *10-15 and 19-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *16-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/3/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

This application is a continuation of 09/889,061 filed 10/22/2001, now US patent 6,645,950 which is a 371 of PCT/GB00/00099 filed 01/14/2000, which claims the foreign priority UNITED KINGDOM 9900752.8 filed 01/15/1999 under 35 U.S.C. 119(a)-(d).

The copy of certified copy of the priority has not been filed with the instant Application.

As indicated in the previous Office Action June 13, 2005, Applicant's preliminary amendment submitted July 3, 2003 is acknowledged wherein the abstract has been amended; Claims 1-9 have been cancelled and claims 10-38 are newly submitted.

Currently, claims 10-38 are pending in this application.

Election/Restrictions

Applicant's election of the invention of Group II, claims 16-18 drawn to a method for treatment or prophylaxis of a solid cancerous tumor in a mammal wherein a composition of Claim 10 is administered to said mammal in a dosage sufficient to damage new vasculature but insufficient to exhibit anti-mitotic activity, submitted July 6, 2005 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is therefore made FINAL.

Claims 11-15 and 19-38 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

As indicated in the previous Office Action June 13, 2005, Claim 10 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 16-18 are examined on the merits herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 16-18 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: the composition in claims 1 and the composition in claim 26 and the composition in claim 30.

Note that claim 10 is withdrawn from further consideration. Insertion of the recitation of composition of claim 10 into claims 32, 36, and 40, respectively, would be favorably considered.

In order to expedite prosecution, claims 16-18 will be examined inserting the recitation of composition of claim 10 into claims 16-18, as have apparently been intended.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-18 are rejected under 35 U.S.C. 112, first paragraph, for scope of enablement because the specification, while being enabling for the treatment of the specific solid cancerous tumor disclosed in the specification by administering the instant compound to said mammal herein, does not reasonably provide enablement for the **prophylaxis** of a solid cancerous tumor.

Note that "**prophylaxis**" is reasonably interpreted as **prevention** according to its ordinary and customary meaning. "Prevention" actually means to anticipate or counter in advance, to keep from happening as defined by Webster's II Dictionary.

The instant claims are drawn to the method for the **prevention** of a solid cancerous tumor in a human or animal. The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims;

(6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

Nature of the invention: The instant invention pertains to the method the prevention of any solid cancerous tumor in a human or animal.

The state of the prior art: The skilled artisan would view that the treatment to prevent solid cancerous tumor in a human or animal totally, absolutely, or permanently, or not even occurring at the first time, is highly unlikely. The skilled artisan would view tumors as a group of maladies (cancers) not preventable with one medicament or therapeutic regimen. Treatment efforts and efforts to treat all tumors (cancers) have produced only isolated identifiable positive results. See *In re Application of Hozumi et al.*, 226 USPQ 353. Moreover, it is well known that so far no single chemotherapeutic agent has been found to be useful in the **prophylaxis** or **prevention** of all known solid cancerous tumors or cancers in a human or animal, or even useful in the treatment of all types of breast cancers; and colon cancers; and prostate cancers. For example, breast cancers and colon cancers do not share a common cause and differ in their methods of treatment, i.e., breast cancers are routinely with estrogens, antiestrogens, and/or androgens, unlike colon cancers, let alone the prophylaxis or prevention thereof.

The relative skill of those in the art: The relative skill of those in the art is high.

The predictability or lack thereof in the art: Note that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In this case, it is

well-known in the state of the art that the cause of a solid cancerous tumor is multifactorial or may be unknown. It is likely that no single factor is responsible to a solid cancerous tumor but rather a variety of factors.

Thus, the skilled artisan would view that the treatment to prevent a solid cancerous tumor in a human or animal totally, absolutely, or permanently by administering a single compound is highly unpredictable, and not even occur at the first time is highly unpredictable.

The amount of direction or guidance presented and the presence or absence of working examples: In the instant case, **no** working examples are presented in the specification as filed showing how to prevent a solid cancerous tumor in a human or animal totally, absolutely, or permanently, not even occurring at the first time. The specification merely provides the testing data of reduction in tumor vascular volume in vitro (see Table 1 in the specification). "Reduction in tumor vascular volume" is considered to be the treatment of a vascular tumor, not prevention at all.

Note that lack of a working example is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art such as the treatment of a solid cancerous tumor. See MPEP 2164.

Genentech, 108 F.3d at 1366, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, as discussed above, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art, Applicants fail to provide information sufficient to practice the claimed invention of the **prophylaxis** of a solid cancerous tumor.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kruse et al. (XP-002142971, PTO-1449 submitted 7/3/03, of record in PCT international search report of the parent case, 09/889,061).

Kruse et al. discloses that the instant specific compounds such as those listed in Table 1 at page 412, Compounds No. 11-28, have antitumor efficacy. The tests on these compounds were conducted *in vitro*. See particular abstract and page 412.

Kruse et al. does not expressly disclose administering the specific compound therein to a patient (e.g., a mammal) in a method for treatment of a solid cancerous tumor in a mammal. Kruse et al. does not expressly disclose that the amount of the specific compound therein in the composition to be administered is from about 0.001-100 mg/kg body weight or 0.1-50 mg/kg body weight.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to administer the specific compound of Kruse et al. to a patient (e.g., a mammal) in a method for treatment of a solid cancerous tumor in a mammal. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the amount of the known compound in about 0.001-100 mg/kg body weight or 0.1-50 mg/kg body weight.

One having ordinary skill in the art at the time the invention was made would have been motivated to administer the specific compound of Kruse et al. to a patient (e.g., a mammal) in a method for treatment of a solid cancerous tumor in a mammal, since these compounds of Kruse et al. are known to have antitumor efficacy in vitro. Therefore, one of ordinary skill in the art would have reasonably expected that these antitumor compounds would have beneficial therapeutic effects and usefulness in methods for treating a solid cancerous tumor in a mammal based on the known in vitro data.

Moreover, regarding *in vitro-in vivo* relationship, one of ordinary skill in the art would allow *in vitro* data to be used as a surrogate for *in vivo* behavior.

One having ordinary skill in the art at the time the invention was made would have been motivated to optimize the amount of the known compound of Kruse et al. to about 0.001-100 mg/kg body weight or 0.1-50 mg/kg body weight based on the known vitro data.

It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

Claims 16-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kruse et al. (XP-002142971, PTO-1449 submitted 7/3/03, of record in PCT international search report of the parent case, 09/889,061).

Nare et al. discloses that the benzimidazoles including instant specific compounds such as Amino-BZ (see its structure at the right column of page 2216), also known as Carbamic acid, [5-(3-aminophenoxy)-1H-benzimidazol-2-yl]-, methyl ester, are potent anti-tumor or anit-neoplastic agents. See in particular abstract, "Results" at page 2217. The tests on these compounds were conducted *in vitro* (see Fig 2 at page 2217).

Nare et al. does not expressly disclose administering the specific compound therein to a patient (e.g., a mammal) in a method for treatment of a solid cancerous tumor in a mammal. Nare et al. does not expressly disclose that the amount of the specific compound therein in the composition to be administered is from about 0.001-100 mg/kg body weight or 0.1-50 mg/kg body weight.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to administer the specific compound of Nare et al. to a patient (e.g., a mammal) in a method for treatment of a solid cancerous tumor in a mammal. It would have been obvious to a person of ordinary skill in the art at the time the invention was

made to employ the amount of the known compound in about 0.001-100 mg/kg body weight or 0.1-50 mg/kg body weight.

One having ordinary skill in the art at the time the invention was made would have been motivated to administer the specific compound of Nare et al. to a patient (e.g., a mammal) in a method for treatment of a solid cancerous tumor in a mammal, since these compounds of Nare et al. are known to be potent anti-tumor agents in vitro.

Therefore, one of ordinary skill in the art would have reasonably expected that these antitumor compounds would have beneficial therapeutic effects and usefulness in methods for treating a solid cancerous tumor in a mammal based on the known in vitro data.

Moreover, regarding *in vitro-in vivo* relationship, one of ordinary skill in the art would allow *in vitro* data to be used as a surrogate for *in vivo* behavior.

One having ordinary skill in the art at the time the invention was made would have been motivated to optimize the amount of the known compound of Nare et al. to about 0.001-100 mg/kg body weight or 0.1-50 mg/kg body weight based on the known vitro data.

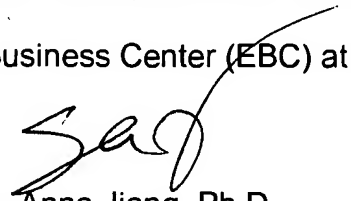
It has been held that it is within the skill in the art to select optimal parameters, such as amounts of ingredients, in a composition in order to achieve a beneficial effect. See *In re Boesch*, 205 USPQ 215 (CCPA 1980).

In view of the rejections to the pending claims set forth above, no claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
September 12, 2005